## REMARKS

Applicants respectfully request reconsideration. By this amendment, Applicants hereby amend claim 45 without disclaimer or prejudice. No claims have been canceled or added. As a result, claims 45-47, 52, and 94-100 are still pending for examination with claim 45 being an independent claim. Basis for the amendment can be found throughout the specification. No new matter is added.

### Rejection Under 35 U.S.C. 112

Claims 45-47, 52 and 94-100 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The Examiner considered the nature of the claimed invention and addressed the enablement of the claims in view of the Wands factors.

The Examiner indicated that the invention is drawn to "a *method of treating or eliminating a tumor or cancer in a subject with an immune system deficiency*." The Examiner then stated that the working examples "do not demonstrate a successful *method of treating or eliminating a tumor or cancer in a subject with an immune system deficiency*" and that "[t]he specification fails to support a correlation between the working examples and claimed methods."

Applicants respectfully disagree. However, Applicants have amended the claims to recite "boosting the immune system in a subject having an immune system deficiency associated with a tumor or cancer." Applicants respectfully submit that this amendment overcomes the rejection, because the specification teaches that oligonucleotides containing an unmethylated CpG dinucleotide produce an immune response that would be useful for a subject with an immune system deficiency, including in a subject having a cancer or tumor. In addition, Applicants have taught routes of administration. Applicants have provided numerous examples of oligonucleotides falling within the genus of molecules recited in the claims. Significant amounts of data demonstrating the effects of CpG oligonucleotides are provided in the specification. The data confirms the effectiveness of the claimed motif by showing that oligonucleotides having an unmethylated CpG dinucleotide are capable of inducing an immune response whereas

oligonucleotides having the same sequence of nucleotides but a methylated C instead of an unmethylated C lose activity.

In the specification, Applicants have demonstrated that oligonucleotides containing an unmethylated CpG are effective at stimulating B-cell proliferation (Table 1), IgM secretion (page 24, IL-6 production (pages 22-26, and Tables 3-4), induction of TNF-α (pages 26-29, and Tables 5-7), induction of IL-12 (pages 26-27, and Table 5), induction of IFN-γ (pages 26-29, and Tables 5-6), induction of GM-CSF (pages 27-29, and Tables 5-7), and induction of NK Cell Stimulatory Activity (pages 32-35, and Tables 8-10). Applicants submit that the description and the data found in the specification establish a pattern of immune stimulation which is beneficial for a subject having an immune system deficiency, including a subject having a cancer or tumor.

The Examiner also pointed to the recitation on page 2673 in Bodey et al. (Anticancer Research 20, 2665-2676, (2000)) that "[m]alignant tumors undergo constant microevolution." The Examiner indicated on page 3 of the Office Action that "the ordinary artisan cannot predict which ODNs to make/use in performing a method of treating or eliminating a tumor in a subject with an immune system deficiency. The constant microevolution is not addressed in the specification."

In response, Applicants respectfully submit that the CpG nucleic acids of the invention act by stimulating an immune response in a subject to which they are administered regardless of whether a malignant tumor in the subject is undergoing microevolution. For example, a CpG nucleic acid being administered does not need to be tailored to a particular antigen on the tumor. Rather, a CpG nucleic acid of the invention is useful for boosting the immune system in a subject having an immune system deficiency associated with a tumor or cancer as presently claimed. The CpG nucleic acids promote a pattern of immune stimulation described above that helps boost the immune system of the subject. In contrast, Applicants submit that the "constant microevolution" reported on page 2673 of Bodey et al., and referred to on page 3 of the Office Action, is described in the context of vaccine therapies based on tumor antigens. The same paragraph of Bodey et al. (see the bottom of page 2673 through the top of page 2674) reports that the "[u]se of cancer vaccines to stimulate the immune system may be in vain, if the particular

TAAs represented in the vaccine preparation are no longer present on the most advanced subsets of cancer cells." Applicants respectfully submit that the CpG nucleic acids of the invention are useful to boost the immune system of the subject regardless of the particular TAAs that are present on the most advanced subsets of cancer cells. Accordingly, an ordinary skilled artisan does not need to predict or correlate CpG nucleic acids with particular TAAs that are present on a tumor in order to practice the invention.

Therefore, Applicants submit that the cited teachings of Bodey et al. do not undermine the predictability of the present invention.

Accordingly, withdrawal of the rejection of claims 45-47, 52, and 94-100 under 35 U.S.C. §112 is respectfully requested.

## CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

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Respectfully submitted,

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